



D J, B., Sabel, C. E., & K, L. (2009). Uncertainty in epidemiology and health risk assessment. *Environmental Geochemistry and Health*, 31(2), 189. <https://doi.org/10.1007/s10653-008-9214-5>

Peer reviewed version

Link to published version (if available):  
[10.1007/s10653-008-9214-5](https://doi.org/10.1007/s10653-008-9214-5)

[Link to publication record in Explore Bristol Research](#)  
PDF-document

## University of Bristol - Explore Bristol Research

### General rights

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available:  
<http://www.bristol.ac.uk/red/research-policy/pure/user-guides/ebr-terms/>

# Uncertainty in epidemiology and health risk and impact assessment

David J. Briggs · Clive E. Sabel · Kayoung Lee

Received: 5 May 2008 / Accepted: 11 September 2008  
© Springer Science+Business Media B.V. 2008

**Abstract** Environmental epidemiology and health risk and impact assessment have long grappled with problems of uncertainty in data and their relationships. These uncertainties have become more challenging because of the complex, systemic nature of many of the risks. A clear framework defining and quantifying uncertainty is needed. Three dimensions characterise uncertainty: its nature, its location and its level. In terms of its nature, uncertainty can be both intrinsic and extrinsic. The former reflects the effects of complexity, sparseness and nonlinearity; the latter arises through inadequacies in available observational data, measurement methods, sampling regimes and models. Uncertainty occurs in three locations: conceptualising the problem, analysis and communicating the results. Most attention has been devoted to characterising and quantifying the analysis—a wide range of statistical methods has been developed to estimate analytical uncertainties and model their propagation through the analysis. In complex systemic risks, larger uncertainties may be associated with conceptualisation of the problem and communication of the analytical results, both of which depend on the perspective and viewpoint of the observer. These imply using more participatory approaches to investigation, and more qualitative measures of uncertainty,

not only to define uncertainty more inclusively and completely, but also to help those involved better understand the nature of the uncertainties and their practical implications.

**Keywords** Uncertainty · Conceptualising · Epidemiology · Health risk

## Introduction

Uncertainty is integral to every human endeavour, and is reflected in the stochastic nature of most real-world events. Attempts to identify, assess and control uncertainties are therefore crucial in trying to understand the world, or predict how it might behave—and as such are basic components of all science. Equally, uncertainty conditions our ability to manage the world, either to reduce unwanted risks or to enhance the human condition. Rarely, if ever, is it possible to remove uncertainty entirely, though many disciplines have developed a range of methods and tools for identifying, characterising and estimating uncertainty, and these provide the basis for at least partial control. Problems of uncertainty nevertheless tend to be most severe in interdisciplinary contexts. One reason is that these areas often lie at the margins of knowledge, where genuine gaps in data and understanding exist. Another is that the issues dealt with are typically complex and multifaceted. A third, not insubstantial, reason is that the different

---

D. J. Briggs (✉) · C. E. Sabel · K. Lee  
Department of Epidemiology and Public Health, Imperial  
College London, Norfolk Place, London W2 1PG, UK  
e-mail: d.briggs@imperial.ac.uk

disciplines involved often have different constructs of uncertainty, and use different language to describe it, so that ambiguities and misunderstandings arise in trying to communicate information on uncertainty.

Problems of uncertainty are therefore especially significant in areas of epidemiology and health risk or impact assessment. Epidemiology is concerned with understanding distributions of disease and its causes, and as such seeks explanations not only in the biological processes that act as proximal determinants of human health, but also the more distal risk factors arising from the environment and society. Epidemiology thus needs to draw on a wide range of disciplines, including medical, environmental, social and mathematical sciences.

Health risk and impact assessment are more difficult to define, if only because different concepts and paradigms of each have emerged over recent decades. In its most traditional form, risk assessment has focused on trying to determine the presence or absence (or in some cases degree) of risk to human health associated with environmental or other hazards. Covello and Merkhofer (1993), for example, define it as “a systematic process for describing and quantifying the risks associated with hazardous substances, processes, actions, or events.” In this form, the focus has been narrow, typically considering only one hazard at a time, and paying little regard either to how different exposures may combine to affect health, or to ways in which human behaviours might affect these risks. Renn (1998), amongst others, highlighted the inadequacies of this approach. More recently, therefore, attempts have been made to develop more comprehensive approaches to risk assessment, under a variety of different names and on the basis of somewhat different principles. Amongst others, these include integrated risk assessment (Bridges 2003; Suter et al. 2005), strategic risk assessment (Slater and Jones 1999) and comparative risk assessment (Murray et al. 2005). In parallel, methods of health impact assessment (Joffe and Mindell 2002; Kemm 2005) have also been developed. These differ from risk assessment in two important ways: they are specifically concerned with the health consequences of policy or other interventions, and thus are focused on change; and in this context they consider both positive and negative effects of interventions, and try to assess the balance of these different effects in order to guide decision making. In addition, over recent

years, the practice of integrated assessment has emerged as “an interdisciplinary and participatory process of combining, interpreting and communicating knowledge from diverse scientific disciplines to allow a better understanding of complex phenomena” (Rotmans and van Asselt 1996). Though as yet applied in only a limited way to health issues, this has been widely used to analyse global problems such as climate change and long-range air pollution, and has been adopted by the European Environment Agency to underpin environmental assessment and reporting (European Environment Agency 2005).

Despite these many differences in name and approach, almost all forms of assessment have a number of commonalities. One is their concern with environmental effects on health (i.e. the effects of environmental hazards and conditions, or of other factors that operate via the environment); another is their multidisciplinary—their reliance on evidence from toxicology, epidemiology, environmental sciences and a wide range of attendant disciplines. A third, crucial point of contact is the importance in all forms of assessment of uncertainty. Indeed, in many ways this has become a more serious concern as the science of assessment has progressed, for whilst methods of analysis and data sources have improved on the one hand, the complexity of the problems being addressed has grown on the other. In the context of these modern, systemic risks (Renn and Klinke 2006), therefore, assessment faces far more difficult challenges, often involves the use and linkage of sophisticated models, and provides the opportunity for the development and propagation of profound forms of uncertainty.

In the light of this, there is a continuing need to try to establish a more coherent and shared understanding of what uncertainty is, how it arises, how it can be identified and assessed and what its implications are. This paper endeavours to contribute to this understanding, in the specific context of geochemical hazards and health. It draws on a number of sources: a review of literature on epidemiology, assessment and uncertainty over the last 10–15 years; thinking on the issue of assessment and uncertainty in two European Union (EU)-funded projects (INTARESE and HEIMTSA); and discussions at a workshop organised as part of the Natural Environment Research Council (NERC)-funded MULTITUDE project in Liverpool in June 2007. Based on these

studies, it presents a framework for uncertainty in environmental epidemiology and risk/health impact assessment, describes and illustrates how uncertainties may arise and propagate in the risk assessment process and outlines ways in which the different types of uncertainty may be specified and quantified.

### A framework for uncertainty

At the most general level, uncertainty can perhaps best be regarded as any departure from complete determinism (Walker et al. 2003). Brown (2004) equates it to “imperfect knowledge”. As such, it has many different facets, derives from a wide range of sources and can be characterised in a variety of ways. Amongst others, terms such as ignorance, ambiguity, indeterminacy, variability, unpredictability, error and unreliability are all often used as full or partial synonyms. As a framework for describing uncertainty, however, it is useful to recognise three main dimensions or properties: its nature (what form it takes), its location (where it arises) and its level (the magnitude of the resulting uncertainty) (Walker et al. 2003).

#### Nature of uncertainty

Many different, though overlapping, classifications of the nature of uncertainty have been proposed, often emanating from different disciplines and thus reflecting the specific types of knowledge and data, and theoretical constructs, that pertain in each area. In many of these, however, a fundamental delineation is made between two broad types of uncertainty, albeit under somewhat different names. On the one side is the uncertainty that is intrinsic to the phenomena under consideration; on the other, that which is extrinsic or observational—i.e. a consequence of our inadequate ability to describe, measure or understand the phenomena concerned. Rotmans and van Asselt (2001a, b) thus distinguish between variability and lack of knowledge; Walker et al. (2003) use the terms “variability uncertainty” and “epistemic uncertainty” for the same two forms, respectively. Suter et al. (1987) divide defined uncertainty (relating to the state of the world) from undefined uncertainty (our underlying ignorance). Regan et al. (2002) make a somewhat different distinction between epistemological and

linguistic uncertainty—the former focusing on the way things are perceived and measured, the latter on how we communicate information about what we see.

Here, the terms intrinsic and extrinsic uncertainty are used. The former refers to the inherent properties of the system under consideration and can be seen to derive from three main sources: randomness, sparseness and nonlinearity. Beyond the quantum scale, true randomness is surprisingly uncommon; most systems show a considerable degree of pattern in both time and space, though this is often masked by the inherent complexities or lack of available data. Sparseness is more common: extreme environmental events, such as major floods or industrial accidents are, fortunately, rare. In this situation, however, the system can appear extremely unstable, for each occurrence represents a major departure from the norm, and patterns in their occurrence are difficult to detect because of the small number of observable events set within a dominating background of non-events. Sparseness is especially important in relation to binary phenomena such as health outcomes—and most crucially so in the case of rare outcomes (e.g. many cancers).

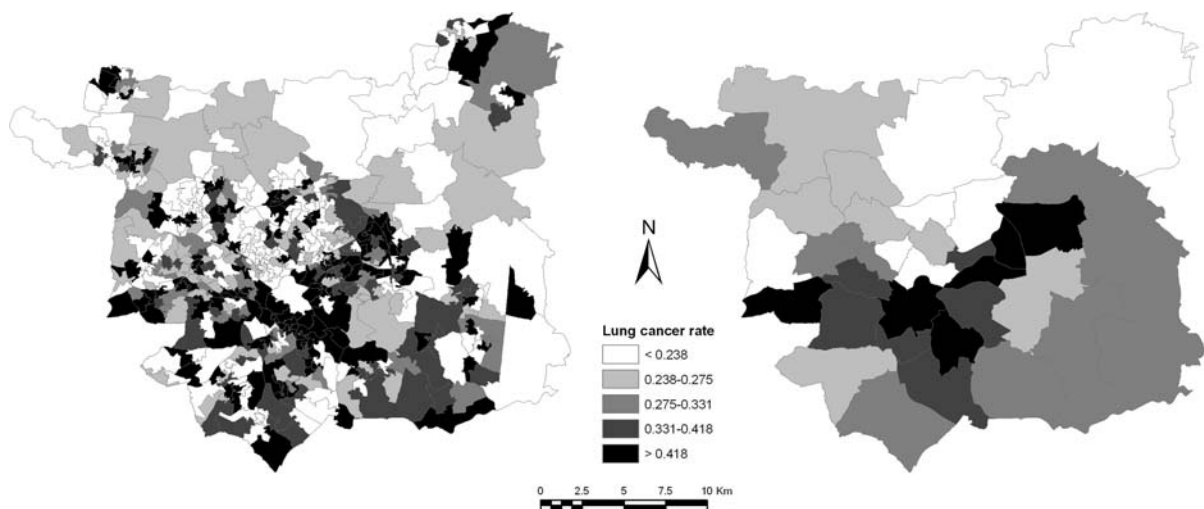
Nonlinearity is also pervasive, and arises for a wide range of reasons. The multidimensionality of the environment, for example, means that dispersion of contaminants is intrinsically a nonlinear function of both distance and time. The self-regulating nature of processes, such as plant uptake of contaminants from the soil, and the self-amplifying nature of many biological processes (e.g. cancer formation), likewise give rise to nonlinear responses. Inelasticity in response may occur because of the buffering capacity of the phenomena concerned (e.g. of soils to acidification, or human organs to exposure to toxins), leading to thresholds or marked curvature in the observed relationships. In the case of health, interactions between different risk factors may also occur, causing so-called effect modification: the health risks of exposure to radon, for example, are known to be exacerbated in the presence of tobacco smoke, apparently because the particulates generated by smoking act as effective carriers for the radon and its daughter products (Barros-Dios et al. 2002); electromagnetic fields (EMF) may act as an effect modifier for exposure to particles, perhaps because they encourage ionisation of fine particulates and thus facilitate their deposition and retention in the airways

(Henshaw 2002). In all these cases, the resulting nonlinearity means that the system may appear to show marked discontinuities in both time and space.

Extrinsic uncertainty relates to imprecision or errors in the observational procedures used to analyse the system. These may derive from every element of the process, including the tools used for observation, the manner in which they are deployed, and the subsequent manipulation and use of the information obtained. Amongst others, therefore, sources of extrinsic uncertainty include the sampling design used to collect data, measurement methods and equipment, statistical methods and models, data recording and transmission, and reading and interpretation of the results.

In practice, intrinsic and extrinsic forms of uncertainty are not wholly independent. As knowledge about how any system is structured and behaves improves, and as our tools for measuring its properties advance, so the system tends to become more predictable and the degree of intrinsic uncertainty appears to decline also. As such the distinction between the two can become extremely tenuous. Brown (2004) thus argues that uncertainty “emerges through the interaction of mind and matter”, and continues: “... people may be uncertain about the environment because: (1) it appears more complex than our abstractions and simplifications imply (complexity); (2) it is too variable for us to capture uniquely (e.g. non-linear or chaotic); (3) it is too large and interconnected for us to observe everything at

once, or too small to observe at all (scale); (4) it is too opaque for us to observe (transparency) or (5) we do not have the capacity to observe it (e.g. no instruments)”. On the one hand, therefore, in a highly regular system, even imprecise measurements or small samples may be sufficient to detect the underlying pattern and make prediction possible. On the other hand, where intrinsic uncertainty is large, imprecision or biases in measurement or sampling make pattern detection—and therefore prediction—even more problematic. One example of this is the so-called small-number problem which often affects health data. Sparse events, when counted at a small-area level (i.e. within small denominator populations), produce rates that are highly variable because each case is rare and each occurrence causes a large change in the observed rate. The noise-to-signal ratio due to chance events is therefore high, and patterns are difficult to detect without the benefit of large data sets. In addition, the disease rates and patterns seen may become highly sensitive to the choice of spatial units used as the basis for the counts—the so-called modifiable areal unit problem (MAUP; Openshaw 1984). In this case, changing from smaller to larger census tracts, for example (Fig. 1), or from census tracts to a regular grid, may result in marked changes in the apparent spatial structure in the data. In Fig. 1, the scale effect component of the MAUP has been demonstrated, using data for Leeds, UK. The same data has been aggregated and then subsequently analysed for two different spatial scales from the UK



**Fig. 1** Lung cancer rates at super output areas (SOA) (left) and ward (right) levels, in Leeds, UK

census: super output areas (SOA) and wards. One can readily see differences between the mapped scales in Fig. 1: for example, relatively high rates of lung cancer that emerge in the NE sector of the map at the SOA level, but disappear entirely in the ward-level analysis. We then investigated whether a further analysis based on these two aggregations would reveal variations. Taking the same lung cancer data, and then correlating this with data on tobacco expenditure in 2006 (from CACI), and the income and education domains of the Index of Multiple Deprivation 2004 (IMD 2004), revealed that, as the geographical level of aggregation increased, the relationships between the variables strengthened (Table 1). These aspects of the MAUP illustrate how study design can introduce a source of uncertainty to any ensuing analysis.

#### Location of uncertainty

The location of uncertainty refers to where it arises in the system under consideration, or, more strictly within the portrayal of that system—what Walker et al. (2003) refer to as the *model complex*. Different ways may be proposed to characterise the locations concerned, resulting in a somewhat confusing array of terms—many of them, unfortunately, not well chosen. The term *model uncertainty*, for example, has variously been used to define uncertainties associated with the conceptual framing of the problem or issue, and the quantitative properties of the physical, mathematical or statistical models used to analyse it (Walker et al. 2003). In reality, which locations are most relevant is likely to vary depending on the nature of the system under consideration and the nature of the enquiry. In general terms, however, it may be helpful to define studies in terms of three key phases, each representing different locations for uncertainty: conceptualisation, analysis and communication.

**Table 1** Correlation coefficients for both super output areas (SOA) and wards between lung cancer rates and tobacco expenditure, income and education for Leeds, UK

	Lung cancer rate (SOA)	Lung cancer rate (ward)
Tobacco expenditure	0.369	0.469
Income	−0.443	−0.669
Education	−0.499	−0.815

#### Conceptual uncertainty

Conceptualisation represents the (usually initial) framing of the study. In an epidemiological investigation this is typically encapsulated in the hypothesis to be tested, and is ideally based on some preconceived theory or understanding of the aetiological processes involved. In risk and impact assessment, it comprises the specification of the risks or policy question(s) to be analysed, and the conditions (e.g. scenarios, study areas) under which this will be done. Conceptualisation thus involves deciding where to place the boundaries (conceptually, spatially and temporally) of the analysis, what aspects to include and which to ignore, and, fundamentally, the underlying model of the system under study—the key relationships of interest and the processes that they represent.

Of all sources of uncertainty, conceptual uncertainty has the greatest potential impact due to the variety of possible philosophical and epistemological positions of the investigating researchers. In empiricist science, pre-eminent in modern epidemiology, exposure and risk assessment, the almost unchallenged philosophical approach is that of the positivist paradigm—unprejudiced observation; the separation of “facts” from “values”; and the emphasis on verification to develop general laws. A Popperian critique of empiricism, however, is that observations themselves are theory dependent. Consider for a moment our respective attitudes to quantitative and qualitative methods. We often struggle to assign equal weight to both types of method, due to our conceptions of what is “scientific knowledge”, and “good science”. We have been trained to consider the Kuhnian interpretation of “normal science” empiricism as cumulative, free of values and interests and thus it largely remains unquestioned and is indeed considered a sign of disciplinary maturity—a single dominant paradigm rather than a multiplicity of competing perspectives. A community of scientists is considered to view the world in a particular way. It is this epistemological position itself that potentially closes our minds to alternative perspectives, and thus to acknowledge the scope for conceptual uncertainty.

The scope for uncertainty in conceptualisation is large and its implications pervasive, for the way the issue is conceived inevitably conditions the results of the analysis. In assessing risks or health impacts, for



example, excluding key sources or pathways of exposure or important determinants of susceptibility will mean that effects may be seriously underestimated, no matter how detailed or reliable the subsequent analysis. Similarly, poor specification of the hazard (e.g. the critical source or agent of interest) is likely to lead to substantial exposure misclassification, diluting the power of an epidemiological study and making it more difficult to detect associations with health outcome. One such recent study, in a health and social economic status context, investigated the spatial implications of alternative socioeconomic status (SES) covariate adjustments—the potential uncertainties when worked through to the alternative risk estimates are illuminating (Sabel et al 2007). Likewise, inadequate definition of the relevant health outcomes may bias studies and limit the generalisability of the results. It is, therefore, regrettable that uncertainties associated with conceptualisation often receive rather scant attention, especially in more traditional and reductionist forms of epidemiology or risk assessment, which usually focus on narrower, quantitative aspects of the analysis.

Conceptual uncertainties arise in most studies of real-world systems, if only because these systems are invariably open, with poorly defined and porous boundaries, and are often complex. Ambiguity thus arises both about what factors to include in the study and how to define them. For an analyst, working alone and making the decisions in isolation, these uncertainties may not be evident. They tend to become apparent, however, when the results are shared with others (whether with the referees of the resulting epidemiological paper or the users of the analysis). In both these cases, challenges may arise regarding the inbuilt assumptions. Conceptual uncertainty thus becomes an issue of asking the wrong question. As this implies, one way of safeguarding against these uncertainties is to frame studies more collaboratively—in consultation with other scientists (especially those who may have a different perspective on the problem) and stakeholders who have interests in the results. While such consultations may not eliminate conceptual uncertainties, they should help to reveal them. On this basis, strategies for dealing with the uncertainties may then be devised: for example, by stating the assumptions explicitly and thus specifying the limits of the study, or by carrying out sensitivity analyses to explore the

possible effects of relaxing or changing the underlying assumptions.

### Analytical uncertainty

As this indicates, conceptual ambiguity is often likely to be a major source of uncertainty in epidemiological studies or risk and impact assessments. Analytical uncertainty, however, often attracts more attention—to some degree, perhaps, because of the so-called lamp-post effect: we study what we can more easily see. Because they are part of the analytical process, these sources of uncertainty are more amenable to examination and quantification: for example, by replicating studies, by testing and validating the equipment and models, or by use of statistical methods to model error propagation. The sources of analytical uncertainty are as broad and varied as the study designs and methods used: each and every aspect of analysis is open to uncertainty. Important sources include sampling, measurement and data handling and processing.

Amongst these, sampling is often the most serious, especially in the case of field-based studies. The difficulties arise from the inherent complexity and spatial and temporal variability of the environment (and human populations). Against this background, the challenge is not only to obtain reliable estimates of average conditions across the study area or population of interest, but to be able to represent the variability of the phenomena concerned, i.e. to provide locally (in time and space) representative data. In terms of health, this is vital, for effects of environment on health rarely, if ever, operate at the aggregate level; instead, they are the result of individual responses to personal exposures occurring in specific locations and during specific time periods. Failure to recognise or measure these specific interactions leads to the so-called ecological fallacy—i.e. the (potentially false) assumption that associations observed at group level reflect (causal) relationships operating at the individual level (Greenland and Morgenstern 1989). Three consequences of this fallacy merit special attention. First, because group-level analysis is likely to ignore or underestimate the effects of possible confounding factors (e.g. within-group variations in socioeconomic status or lifestyle), the observed associations may be biased, typically (though not always) away from the null. Second,

because the range of aggregated exposure estimates is likely to be attenuated compared to those at individual level (through the simple process of averaging), risks at the extremes of exposure (both high and low) may be misrepresented. Third, because the differential effects between individuals cannot be observed, the existence of subpopulations of susceptible people, who may be affected at very low levels of exposure, is likely to be missed. Together, these sources of uncertainty make it extremely difficult to interpret results from aggregate-level epidemiological studies, and especially difficult to deduce causal relationships. In the attempt to overcome these problems, epidemiology has tended to turn away from studies using aggregate data, wherever possible, and instead design studies at individual level. Case-control studies, in which health effects in an observed set of exposed individuals are compared with those in a set of unexposed (or less exposed) individuals, is one approach. Cohort studies, in which a group of individuals are followed over time, and their exposures and health outcomes monitored, provides a potentially more powerful (though also more costly) design.

Problems of obtaining representative samples nevertheless affect most studies, not least in relation to exposure estimation. The problems arise because of the cost of sampling and measurement, which mean that, even in well-funded studies, a sufficient number of measurements can rarely be made. These problems apply as much to routine monitoring systems, such as the air pollution networks maintained by national and municipal authorities, as they do smaller, purpose-designed research studies: while the investment in routine monitoring may be larger, the need to cover large areas, maintain networks over the long term and provide high levels of quality assurance all limit the sampling density. Inherent in most attempts at exposure assessment, therefore, is some degree of trade-off between temporal and spatial representivity. The choice is either to increase the number of sampling sites but limit measurement either to long-term averages or brief snapshots in time, or to use fewer sites and monitor variations over time. The choice should, in principle, be driven by the hypothesis about what are the critical averaging times for exposure. In practice, however, other considerations often intervene. Most routine air pollution monitoring networks, for example, are

governed by the prerogative of regulatory compliance. They thus focus on obtaining time-series data (for time intervals consistent with the regulations) and are targeted at known or suspected pollution hotspots. As such, they are likely to provide very biased assessments of exposure—though this has not stopped them being used for this purpose, almost as a gold standard. Purpose-designed studies, on the other hand, often have greater potential for personal monitoring, but are usually severely time and resource limited, and thus tend to take snapshot measurements.

Given the limitations of both routine and purpose-designed monitoring, many epidemiological studies have turned to the use of models for exposure assessment. Indeed, except in those few cases where direct measurements are made on every individual in a study, for the full exposure period of interest, it can be justifiably argued that *all* epidemiological studies involve modelling of exposures. Many, however, use such simple (and naïve) models—e.g. the assumption that the monitored data can be simply extrapolated across the study population—that they are not even recognised as models. Risk and health impact assessments likewise (and usually more explicitly) rely heavily on modelling to extend monitored data to the population at large, and to make predictions of future exposures for relevant assessment scenarios (e.g. different policy options).

Many different approaches to modelling are used for these purposes, but two are perhaps of general applicability. Process models aim to simulate the real-world mechanisms of hazard propagation and exposure; perhaps the most common examples are the dispersion models often used to estimate air pollution concentrations (Colville and Briggs 2000). Similar models are also available, however, for a wide range of other hazards and media, including noise (Heimann 2007; Ploysing 2000; van Maercke and Defrance 2007), electromagnetic radiation (Kürner 2003), stream-water pollution (Rauch et al. 1998), groundwater pollution (Refsgaard et al. 1999), floods (Horritt and Bates 2002; Lamberti and Pilati 1996), geological hazards (Atkinson and Somerville 1994; Carey and Sparks 1986; Hurst and Turner 1999) and vector-borne and communicable diseases (Anderson and Garnett 2000; Rogers et al. 1988). Likewise, demographic models have been developed to simulate both natural population dynamics and local and



interregional migration (Cohen 1986; Lee and Tuljapourkar 1994; Newell 1988; van Imhoff and Post 1998). Process models tend to be deterministic in that they take no direct account of uncertainties in the processes involved, though these may be ascertained independently, for example by carrying out validation studies or sensitivity analyses.

Statistical models, in contrast, attempt to simulate the resulting distribution of exposures without direct recourse to the underlying processes. They are also typically stochastic in design, in that they make a deliberate effort to quantify uncertainties. Two main approaches to statistical modelling have evolved. The traditional approach uses frequentist statistical methods, amongst which regression techniques are perhaps the most commonly applied, especially in the analysis of urban air pollution (Briggs 2007; Briggs et al. 1997, 2000; Jerrett et al. 2005). In more recent years, however, Monte Carlo and Bayesian methods have gained favour (Nieuwenhuijsen et al. 2006). Monte Carlo simulation involves the repeated resampling and analysis of distributions derived either from observational data, or from preconceived assumptions, to model the frequency of events such as exposures across the population. Bayesian analysis takes this approach further, by enabling prior knowledge, and nonquantitative forms of information such as expert judgements, to be incorporated into the analysis (Ramachandran 1999). In these ways, it can provide more robust estimates of exposure, together with more informative descriptions of uncertainties.

Where formal models cannot be developed for exposure assessment, proxies may be used. In occupational epidemiology, for example, information on job category is often employed as a surrogate for exposure (Nieuwenhuijsen 2003); in studies of traffic-related air pollution and health, distance from road or traffic volume on the nearest road have frequently been used (Huang and Batterman 2000). These, essentially, represent a naïve and implicit form of regression model, in that they are based on the assumption of a (usually linear) association between the proxy measure and the exposure of concern. Unfortunately, this assumption is not only often untested, but also in many situations false (Briggs 2005, in press).

The uncertainties that arise in using models to represent real-world systems are widely recognised and have been extensively debated. Major sources include inadequate understanding of the fundamental

processes or relationships being modelled, leading to poor model parameterisation, and inadequacies in the available input data. These problems are perhaps most severe in trying to model human behaviours and responses. One consequence of these uncertainties is that models may display equifinality—in which different representations of reality may match the observed data more-or-less equally (Beven 2002, 2006; Beven and Freer 2001). In the case of risk and impact assessments, moreover, many of these uncertainties are exacerbated by the need to combine and link models in order to represent the full system between source and exposure. Many of the models used are rather poorly validated, especially under the heterogeneous conditions that characterise many real-world systems, while marked nonlinearity may occur at the interfaces between system compartments, where natural regulators may act either to inhibit or amplify transfers. As a consequence, error propagation may also be markedly nonlinear. Where relevant data do exist, it may be possible to mitigate these errors through the use of data assimilation techniques, by which modelled estimates are continuously recalibrated to match the observations before being passed on as inputs to the next stage (Beven and Freer 2001; Romanowicz and Young 2003). Unfortunately, in many cases, data are sparse so the opportunities for corrective measures of this type are limited. Inevitably, therefore, there is the danger that modelled estimates diverge progressively, and in some cases abruptly, from reality as modelling proceeds from source to exposure.

Spatial scale transitions pose similar problems. As already emphasised, exposures to hazards take place at the individual level. The hazards themselves, however, may represent processes which span a range of different scales. Thus, atmospheric particulate pollution represents the consequence of both local and long-range sources acting in combination, as well as the mediating effects of the immediate living environment; heat waves, likewise, involve processes operating at scales from the micro-environmental to the global. Analysis of complex systems therefore frequently requires the use of spatially nested models. Most environmental models are scale specific (Heuvelink 1998). They are typically based on different modelling principles, and have been validated under different conditions, with the aim of maximising their individual, internal consistency.

Applying models at other spatial scales therefore carries the potential for substantial uncertainty. Compatibility of the models across different geographic scales has also rarely been evaluated. As a result, coupling of models may lead to a wide variety of errors, including those of both omission and commission. In the case of atmospheric particulates, for example, it is evident that the interregional component resulting from long-range transport does not simply add to the locally derived particulate fraction, but interacts with it (via nucleation, condensation and coagulation) to change the particle size distribution and both mass and number concentration. Simple summation of concentration estimates from long-range and local dispersion models is therefore likely to be erroneous.

Similar issues occur in relation to time scales. Whilst short-term exposures, with the capability to cause acute health effects, have traditionally attracted most concern, it is now recognised that chronic effects resulting from cumulative (including lifelong) exposures are often a more important public health problem. In reality, however, the two are not independent: on the one hand, long-term exposures may make people more sensitive to acute effects, for example by lowering their susceptibility (Halfon and Hochstein 2002, Lynch and Smith 2005); on the other hand short-term exposures at critical life stages (especially pre- or neonatal) may have lifelong effects (Law and Shiell 1996; Phillips et al. 2000). As a result, exposure modelling often has to span different time scales in order to obtain estimates of their combined effects. In doing so, questions clearly arise about the relevant exposure windows and metrics, and about how to integrate them realistically. This is compounded, particularly (though not uniquely) for long-term exposure, by the problem of case migration, which can result in severe mis-estimation of exposures for individual cases.

In the context of risk and health impact assessment, an additional and specific source of temporal uncertainty arises, namely in defining the time window of exposure in a way that ensures that the full time series of relevant exposures and effects are taken into account. Ideally, this is done by running models for the full lifecycle of the risks or policy interventions—from their initial introduction, through the intervening period of adaptation, to the period of new steady state and thence until the effects

ultimately cease. Any other analysis involves some degree of bias. In practice, this is almost impossible to do. Uncertainties inevitably arise about how long the new situation will be maintained: indeed a common problem with many policy interventions is that they are far more temporary than anticipated, so while the setup costs (which usually occur early in the lifecycle) are paid in full, there is inadequate time to accrue the full benefits. The length of the period of adaptation may also be uncertain—and in many systems a period of static equilibrium is never reached, so change is almost continuous. Issues of latency likewise arise, most especially in relation to congenital or reproductive disorders which may have lifetime or even intergenerational effects.

In terms of the implications of these various sources of uncertainty for the results of any analysis, a distinction needs to be made between differential and nondifferential effects. A common assumption in epidemiology has been that uncertainties in exposure assessment are nondifferential, in that they are not biased towards cases or controls (or towards specific parts of the distribution of disease rates). As such, they should act to reduce the statistical power to detect any association between exposure and health outcome, but should not bias the risk estimates (e.g. the slope of the exposure–response function). For this reason, uncertainties in exposure estimation have often received less attention than other uncertainties, which are considered more likely to be systematic in their effect, such as confounding by socioeconomic factors. The extent to which this assumption is true has been the subject of occasional, though as yet not exhaustive, debate (Blair et al. 2007). Certainly there are situations in which systematic errors in exposure estimation are possible—and indeed likely. Detection limits of monitoring equipment, for example, mean that lower level exposures are likely to be systematically underestimated; dispersion modelling techniques are liable to under- rather than overestimate exposures because they often ignore important emission sources (e.g. long-range contributions from outside the study area); use of distance from source as a proxy for exposure may overestimate exposures at distant, compared with proximal, locations because it ignores the nonlinear (e.g. inverse square) distance decay patterns that actually exist.

In the context of risk and impact assessment, another important source of analytical uncertainty

occurs in terms of the associations between exposure and health effect. Whereas epidemiological studies are generally concerned with trying to elucidate these relationships, risk and impact assessment rely on existing exposure–response or dose–response functions to translate estimates of exposure into estimates of health effect. These functions are, however, subject to a wide variety of uncertainties. To some degree, these uncertainties are explicit in the reported associations (typically as confidence limits around the point estimates of relative risk, excess risk or odds ratios). Less obvious, are the uncertainties inherent in trying to obtain best estimates from the (often diverse) published data, for a specific assessment. Differences in the reported functions, for example, occur because of many, often hidden differences in study design—in the specific nature of the hazards investigated, in the exposure metrics and models, in the size and characteristics of the study population, in the statistical and other methods used for analysis and in the characterisation and reporting of the health outcomes. Different studies also differ in terms of their reliability and statistical power, so not all reported exposure–response functions can be treated as equal. In addition, publication biases tend to favour reporting of positive findings. Using a simple average of the reported estimates is thus likely to be misleading. Taking results from the most local study, on the grounds that this will best represent the conditions and population in the study area, might seem more appropriate, but places reliance on a single study, which on its own has limited statistical power. Combining data from different studies to derive exposure–response functions for specific applications is thus fraught with difficulties. Pooled analyses, in which the data themselves are combined and reanalysed, is often regarded as the optimum approach, but is not always feasible due to difficulties of access to the relevant data (or summary statistics) and the resource implications. Systematic reviews, selecting and weighting findings from different studies on the basis of clear, predefined criteria, may be more practicable but again need to be based on clear selection criteria.

In terms of impact assessments, also, the computed effects of any policy or other intervention need to be translated into estimates of impact—e.g. in terms of changes in mortality, morbidity or some measure of the overall burden of disease. Such calculations depend on knowing the background disease or

mortality rates for the diseases of interest. These, too, often involve uncertainties, which vary over both space and time, due to differences in referral practices, diagnosis or reporting; commonly, for example, the registries that collect data on notifiable diseases such as birth defects or cancers vary in their efficiency, creating marked (but spurious) differences in reported disease rates (Baron and Weiderpass 2000). Estimates of the overall disease burden also depend on being able to combine different health outcomes into a single metric of health status. These need to reflect differences in both the duration and severity of the diseases, as well as their prevalence. Amongst others, metrics such as disability-adjusted life years (DALYs), quality-adjusted life years or monetary measures have been used. Each of them suffers from uncertainties in the way in which different health outcomes are weighted in terms of their severity (Anand and Hanson 1997; Barker and Green 1996; Edejer et al. 2003; Gold et al. 2002). For diseases with long-term consequences, or which have delayed effects, problems also arise in weighting (i.e. discounting) future compared with immediate effects.

#### Communicational uncertainties

The final stage of risk and impact assessment comprises communication of the results. The way in which this is done varies greatly, depending on the nature of the problem, the roles of those involved and perceptions of the needs of the participants. Many of these participants are inevitably nonspecialists, and as such are likely to have difficulties in dealing with the complex, and often jargonised, information that emerges from epidemiological studies or risk assessments. For this reason, scientists are commonly exhorted to use simpler terms or analogies to communicate their findings. In many cases, also, results of risk or impact assessments are presented in the form of indicators: simplified representations (i.e. signals) of the key messages that need to be imparted. Constructing meaningful indicators, however, is extremely challenging, for simplification inevitably comes at the cost of loss of information. Many indicators and analogies thus imply approximation and ambiguity, and in many cases they may bias the knowledge that is transmitted.

As already noted, risk communication is also not merely a matter of telling stakeholders what the risks

or impacts are; it implies a much more interpretive process, in which the meaning and validity of the results can be considered, and their implications discussed. In practice, this is rarely achievable through a post hoc presentation of, and discussion about, the results of the analysis. Indeed, in many situations this is likely to encourage suspicion or hostility amongst the recipients, who may rightly feel that they are being treated as a passive audience rather than real stakeholders in the risks. Since one of the aims of risk communication is to gain support for whatever actions are necessary, and to promote an appropriate collective response from those involved, such attitudes are likely to prove counterproductive. If communication is to be effective, therefore, it needs to be a far more equal and participatory process. If stakeholders are to bring their own interests and experience to bear on the analysis, it also needs to start early in the process—at the stage of issue framing.

As with all discourse, risk communication and stakeholder participation is fraught with uncertainties. These arise on both sides of the discourse: in the originator's understanding of the issue, and their access to relevant words or symbols to represent it, and in the receiver's own intelligence, education, experience, imagination and linguistic or visual capabilities. The dilemma, with particular relevance to uncertainty, is captured in the oft quoted (and misunderstood):

“... as we know, there are known knowns; there are things we know we know. We also know there are known unknowns; that is to say we know there are some things we do not know. But there are also unknown unknowns—the ones we don't know we don't know.” *Donald Rumsfeld (former US Defense Secretary) 12th February 2002*

Differences in technical knowledge, compounded in many cases by the jargon or specialist terms involved, often exacerbate this problem. Distrust, or the sense of powerlessness, may also bias people's interpretations, and make it even more difficult to establish consensus across the stakeholders involved.

The resulting uncertainties are, by definition, difficult to identify or assess, because they are invariably implicit and cannot usually be tested against independent observations. At best they

emerge as a mismatch between how people behave in response to the information and how they might have been expected to respond. In most cases, therefore, there is no real substitute for a deeper discourse if real understanding is to be achieved. This needs to use a range of different methods, both to reinforce understanding by trying to minimise the ambiguities inherent in any specific mode, and to deal with the different levels of expertise, and different preconceptions and needs, of different stakeholders. An important rule of risk communication is thus that one mode of communication is rarely sufficient. Use of multiple modes, however, requires that these are consistent, if confusion is to be avoided. All these problems are further compounded by the multitude of stakeholders who may have interests in many situations, especially those which are complex and systemic in nature. Indeed, in these situations, even defining stakeholders can be problematic (Briggs and Stern 2007). If it is to be effective, therefore, risk communication is by necessity a time-consuming process. It also has to be planned well in advance. It is too late to try to identify, contact and assemble the relevant stakeholders after a problem has emerged. Instead, organisations with responsibility for risk governance need to build up links with their constituencies on a long-term basis.

### Magnitude of uncertainty

Whilst knowledge about the location and nature of uncertainties in epidemiological analyses or risk and impact assessments is clearly valuable, ultimately the main concern is with the level or magnitude of the uncertainties. This implies the ability both to quantify and communicate the uncertainty (in addition to the risks to which they relate).

In order to provide a general framework for describing levels of uncertainty, Walker et al. (2003) present a spectrum from full determinism (no uncertainty) to total ignorance. Within this, so-called statistical uncertainty is seen to arise where some degree of quantification of the system is possible, such that the probability of different outcomes can be assessed. Potential errors are thus definable at least stochastically, and traditional statistical tools, such as confidence intervals, can be used. In situations where the outcomes can be defined, but their probability of occurrence is

unknown, the term *scenario uncertainty* is used (somewhat unfortunately, because the uncertainties do not necessarily originate in the definition or modelling of the scenario). In this case, uncertainties are often represented by providing best- and worst-case estimates (or upper and lower projections). These are inherently less informative than confidence intervals because they tell nothing about the probability distributions involved. Beyond this, Walker et al. (2003) define *recognised ignorance* as the state in which the potential for an effect is known, but neither the direction nor probability of the effect can be assessed because the underlying mechanisms and relationships are not understood. Total ignorance relates to the condition of not even knowing what we do not know, implying that the system is totally indeterminate (and thus appears to behave randomly).

This classification of levels of uncertainty has considerable value by drawing attention to the epistemological context within which knowledge exists. As a basis for communicating information on uncertainty, however, it is clearly limited. For this, more normative (though also flexible and imaginative) techniques are required. Where they are possible, quantitative measures, such as confidence intervals or probability statements, are obviously useful in this respect. Crude, aggregate measures of uncertainty, however, can hide the fact that levels of uncertainty often vary across the study area or population—for example, because of differences in sample density or the quality of the input data to models. In this context, mapping of uncertainties can be informative. With the use of geographic information systems, interactive mapping is now possible. Pebesma et al. (2007), for example, describe a system developed in the Aguilla software, which enables interactive interrogation of uncertainties by, *inter alia*, passing a cursor over the map and extracting information on the probability distribution at each location, or defining confidence limits as thresholds for mapping (e.g. showing only areas that exceed a specified confidence limit).

Where full quantification of the level of uncertainty is not feasible, more qualitative methods may still provide considerable insight. One approach is to use Likert-type scales to score different types or sources of uncertainty on a range from negligible to serious (or overwhelming). Another is to rank sources of uncertainty relative to each other, or to a well-

known and defined reference phenomenon, such as the daily weather forecast. Diagrammatic measures, such as simple bubble graphs or spider diagrams, can similarly be used to convey broad qualitative information about uncertainty to lay users. In the same way, it can be helpful to construct system diagrams to represent the factors and relationships considered in the analysis, and to attribute this (e.g. via colours or variations in line thickness) to indicate relative levels of uncertainty. Narratives, too, can be powerful means to convey and discuss uncertainties, not just in a static descriptive sense as an attribute of the result of the analysis, but much more informatively by exploring how the uncertainties arose and their potential implications. Whatever approach is used, it is important to bear one thing in mind: the purpose of measuring and reporting uncertainty in epidemiology or risk assessment is to aid understanding of the phenomena concerned, and to improve decision making. The needs, capabilities and perceptions of the users are thus crucial both in defining what aspects of uncertainty matter, and to what degree, and in determining how it can most effectively be described and reported.

## Conclusions

In recent years it has become common to emphasise the need to understand and report uncertainty much more systematically in epidemiological studies and in assessments of risk or health impact. Methods to achieve this have, nevertheless, been slow to emerge. Most attention to date has also focused on statistical techniques for modelling the propagation of uncertainties, and for describing their magnitude. Deeper consideration suggests that uncertainty is much more than a statistical issue: it relates also to the way we perceive, interact with and use the world. Purely statistical approaches to uncertainty analysis also tend to exclude the many situations in which quantification is either infeasible or inappropriate. Equally, the reification of uncertainties by statistical means may in some cases make the issue of uncertainty less clear, rather than more transparent, for many users. Uncertainty analysis thus needs to be seen as a much more participatory and formative activity—one that permeates the whole process of investigation or assessment from initial issue framing to ultimate interpretation



and exploitation of the results. By the same token, it also needs to be regarded as a participatory process. This is essential not only in order to help those involved better understand the uncertainties, but also because uncertainty only has meaning in relation to the issue and the users concerned. High levels of uncertainty (in a statistical sense) may matter little, for example, if the system under consideration is largely resilient to influence, or if the effects of any intervention offer negligible benefits and carry little cost. On the other hand, even minute degrees of uncertainty can be devastating in tightly engineered systems and where consequences of error are large (or are perceived to be so). Uncertainty thus needs to be seen as much more than an attribute of real-world systems or of our analytical methods. Crucially and fundamentally it is a social phenomenon, tied up with the perceptions, expectations, needs, behaviours and well-being of those who have a stake in the associated risks. Ultimately, therefore, uncertainty belongs to the user, not to the analyst.

**Acknowledgements** This paper arose out of multidisciplinary discussions held at the MULTITUDE/SEGH workshop, held in June 2007 in Liverpool, UK. Participants with a wide range of expertise were brought together with the author(s) and this interpretation owes a great deal to those resultant discussions. The participants in this particular theme of the workshop included Louise Ander, Katy Boon, Paul Cleary, Elisa Giubilato, James Grellier, Gibby Koshy, Maria Lathouri, Paolo Luria, George Onuoha, Lesley Rushton, Tom Shepherd and Chaosheng Zhang. This research and the workshop was supported by The Joint Environment & Human Health Programme, supported by the Natural Environment Research Council (NERC), Department for Environment, Food & Rural Affairs (Defra), Environment Agency (EA), Ministry of Defence (MOD), Economic & Social Research Council (ESRC), Medical Research Council (MRC), Biotechnology & Biological Sciences Research Council (BBSRC), Engineering & Physical Sciences Research Council (EPSRC), Health Protection Agency (HPA), and administered via NERC grant NE/E009484/1. The authors also gratefully acknowledge funding from the European Union, through the 6th Framework Programme INTARESE and HEIMTSA studies, for the work underlying the views presented here.

## References

- Anand, S., & Hanson, K. (1997). Disability-adjusted life years: A critical review. *Journal of Health Economics*, 16, 685–702.
- Anderson, R. M., & Garnett, G. P. (2000). Mathematical models of the transmission and control of sexually transmitted diseases. *Sexually Transmitted Diseases*, 77(10), 617–626.
- Atkinson, G. M., & Somerville, P. G. (1994). Calibration of time history simulation methods. *Bulletin of the Seismological Society of America*, 84(2), 400–414.
- Barker, C., & Green, A. (1996). Opening the debate on DALYs. *Health Policy and Planning*, 11, 179–183.
- Baron, J. A., & Weiderpass, E. (2000). An introduction to epidemiological research with medical databases. *Annals of Epidemiology*, 10, 200–204.
- Barros-Dios, J. M., Barreiro, M. A., Ruano-Ravina, A., & Figueiras, A. (2002). Exposure to residential radon and lung cancer in Spain: A population-based case-control study. *American Journal of Epidemiology*, 156, 548–555.
- Beven, K. (2002). Towards a coherent philosophy for modelling the environment. *Proceedings of the Royal Society of London Series A*, 458, 2465–2484.
- Beven, K. (2006). A manifesto for the equifinality hypothesis. *Journal of Hydrology*, 320, 18–36.
- Beven, K., & Freer, J. (2001). Equifinality, data assimilation, and uncertainty estimation in mechanistic modelling of complex environmental systems using the GLUE methodology. *Journal of Hydrology*, 249, 11–29.
- Blair, A., Stewart, P., Lubin, J. H., & Forastiere, F. (2007). Methodological issues regarding confounding and exposure misclassification in epidemiological studies of occupational exposures. *American Journal of Industrial Medicine*, 50, 199–207.
- Bridges, J. (2003). Human health and environmental risk assessment: The need for a more harmonised and integrated approach. *Chemosphere*, 52, 1347–1351.
- Briggs, D. J. (2005). The role of GIS: Coping with space (and time) in air pollution exposure assessment. *Journal of Toxicology and Environmental Health A*, 68(13–14), 1243–1261.
- Briggs, D. J. (2007). The role of GIS to evaluate traffic-related pollution. Editorial. *Occupational and Environmental Medicine*, 64, 1–2.
- Briggs, D. J., Collins, S., Elliott, P., Kingham, S., Fisher, P., Lebre, W., et al. (1997). Mapping urban air pollution using GIS: A regression-based approach. *International Journal of Geographical Information Science*, 11(7), 699–718.
- Briggs, D. J., de Hoogh, C., Gulliver, J., Wills, J., Elliott, P., Kingham, S., et al. (2000). A regression-based method for mapping traffic-related air pollution: Application and testing in four contrasting urban environments. *Science of the Total Environment*, 253, 151–167.
- Briggs, D. J., de Hoogh, C., & Gulliver, J. (in press). Matching the metric to need: modelling exposures to traffic-related air pollution for policy support. *Journal of Toxicology and Environmental Health*.
- Briggs, D. J., & Stern, R. (2007). Effective management of risk response—towards an ecological approach. *Journal of Risk Research*, 10(5–6), 593–622.
- Brown, J. D. (2004). Knowledge, uncertainty and physical geography: Towards the development of methodologies for questioning belief. *Transactions of the Institute of British Geographers*, 29(3), 367–381.
- Carey, S., & Sparks, R. S. J. (1986). Quantitative models of the fallout and dispersal of tephra from volcanic eruption columns. *Bulletin of Volcanology*, 48, 109–125.



- Cohen, J. E. (1986). Population forecasts and confidence intervals for Sweden: A comparison of model-based and empirical approaches. *Demography*, 23, 105–126.
- Colville, R., & Briggs, D. J. (2000). Dispersion modelling. In P. Elliott, N. Best, J. Wakefield & D. J. Briggs (Eds.), *Spatial epidemiology: Methods and applications* (pp. 375–392). Oxford: Oxford University Press.
- Covello, V. T., & Merkhofer, M. W. (1993). *Risk assessment methods. Approaches for assessing health and environmental risks* (p. 318). New York: Plenum.
- Edejer, T. T.-T., Baltussen, R., Adam, T., Hutubessy, R., Acharya, A., Evans, D. B., et al. (2003). *Making choices in health. WHO guide to cost-effectiveness analysis*. Geneva: World Health Organisation.
- European Environment Agency. (2005). *The European Environment—State and outlook*. Luxembourg: Office for Official Publications of the European Communities.
- Gold, M. R., Stevenson, D., & Fryback, D. G. (2002). HALYS and QALYS and DALYS, oh my: similarities and differences in summary measures of population health. *Annual Review of Public Health*, 23, 115–134.
- Greenland, S., & Morgenstern, H. (1989). Ecological bias, confounding, and effect modification. *International Journal of Epidemiology*, 18, 269–274.
- Halfon, N., & Hochstein, M. (2002). Life course health development: an integrated framework for developing health, policy and research. *The Millbank Quarterly*, 80, 433–479.
- Heimann, D. (2007). Three-dimensional linearised Euler model simulations of sound propagation in idealised urban situations with wind effects. *Applied Acoustics*, 68, 217–237.
- Henshaw, D. (2002). Does our electricity distribution system pose a serious risk to public health? *Medical Hypotheses*, 59, 39–51.
- Heuvelink, G. B. M. (1998). Uncertainty analysis in environmental modelling under a change of spatial scale. *Nutrient Cycling in Agroecosystems*, 50, 255–264.
- Horritt, M. S., & Bates, P. D. (2002). Evaluation of 1D and 2D numerical models for predicting river flood inundation. *Journal of Hydrology*, 268, 87–99.
- Huang, Y.-L., & Batterman, S. (2000). Residence location as a measure of environmental exposure: a review of air pollution epidemiology studies. *Journal of Exposure Analysis and Environmental Epidemiology*, 10, 66–85.
- Hurst, A. W., & Turner, R. (1999). Performance of the program ASHFALL for forecasting ashfall during the 1995 and 1996 eruptions of Ruapehu volcano. *New Zealand Journal of Geology and Geophysics*, 42, 615–622.
- Jerrett, M., Arain, A., Kanaroglou, P., Beckerman, B., Potoglou, D., Sahsuvaroglu, T., et al. (2005). A review and evaluation of intraurban air pollution exposure models. *Journal of Exposure Analysis and Environmental Epidemiology*, 15, 185–204.
- Joffe, M., & Mindell, J. (2002). A framework for the evidence base to support health impact assessment. *Journal of Epidemiology and Community Health*, 56, 132–138.
- Kemm, J. (2005). The future challenges for HIA. *Environmental Impact Assessment Review*, 25, 799–807.
- Kürner, T. (2003). Propagation models for macro-cells. In E. Damosso & L. M. Correia (Eds.), *Digital mobile radio: towards future generation systems. COST 231 Final Report* (pp. 134–148). Luxembourg: Office for Official Publications of the European Communities.
- Lamberti, P., & Pilati, S. (1996). Flood propagation models for real-time forecasting. *Journal of Hydrology*, 175, 239–265.
- Law, C. M., & Shiell, A. W. (1996). Is blood pressure inversely related to birth weight? The strength of evidence from a systematic review of the literature. *Journal of Hypertension*, 14, 935–941.
- Lee, R. D., & Tuljapurkar, S. (1994). Stochastic population forecasts for the United States: Beyond high, medium, and low. *Journal of the American Statistical Association*, 80, 1174–1189.
- Lynch, J., & Smith, G. D. (2005). A life course approach to chronic disease epidemiology. *Annual Review of Public Health*, 26, 1–35.
- Murray, C. J. L., Ezzati, M., Lopez, A. D., Rodgers, A., & Vander Hoorn, S. 2005. Comparative quantification of health risks: Conceptual framework and methodological issues. Population Health Metrics 1. Available at: <http://www.pophealthmetrics.com/content/1/1/1>.
- Nieuwenhuijsen, M. (Ed.). (2003). *Exposure assessment in occupational and environmental epidemiology*. Oxford: Oxford University Press.
- Nieuwenhuijsen, M., Paustenbach, D., & Duarte-Davidson, R. (2006). New developments in exposure assessment: The impact on the practice of health risk assessment and epidemiological studies. *Environment International*, 32, 996–1009.
- Newell, C. (1988). *Methods and models in demography* (p. 217). New York: Guilford.
- Openshaw, S. (1984). *The modifiable areal unit problem. CATMOG No 38*. Norwich: Geo Books.
- Pebesma, E. J., de Jong, K., & Briggs, D. (2007). Interactive visualization of uncertain spatial and spatio-temporal data under different scenarios: An air quality example. *International Journal of Geographical Information Science*, 21(5), 515–527.
- Phillips, D. I. W., Walker, B. R., Reynolds, R. M., Flanagan, D. E. H., Wood, P. J., Osmond, C., et al. (2000). Low birth weight predicts elevated plasma cortisol concentrations in adults from 3 populations. *Hypertension*, 35, 1301–1306.
- Ploysing, B. 2000. Nord2000: Comprehensive outdoor sound propagation model. Part 2. Propagation in an atmosphere with refraction. Report to Nordic Noise Group, AV1851/00. Lyngby: DELTA.
- Ramachandran, G. (1999). Retrospective exposure assessment using Bayesian methods. *Annals of Occupational Hygiene*, 45r, 651–667.
- Rauch, W., Henze, M., Koncsos, L., Reichert, P., Shanahan, P., Somlyódy, L., et al. (1998). River water quality modelling: I State of the art. *Water Science and Technology*, 38(11), 237–244.
- Refsgaard, J. C., Thorsen, M., Jensen, J. B., Kleeschulte, S., & Hansen, S. (1999). Large scale modelling of groundwater contamination from nitrate leaching. *Journal of Hydrology*, 221, 117–140.
- Regan, H. M., Colyvan, M., & Burgman, M. A. (2002). A taxonomy and treatment of uncertainty for ecology and conservation biology. *Ecological Applications*, 12, 618–628.

- Renn, O. (1998). Three decades of risk research: accomplishments and new challenges. *Journal of Risk Research*, 1, 49–71.
- Renn, O., & Klinke, A. (2006). Systemic risks as challenge for policy making in risk governance. Forum: Qualitative Social Research, 7, 33 pp.
- Rogers, D. J., Onstad, D. W., & Killick-Kendrick, R. (1988). The dynamics of vector-transmitted diseases in human communities [and Discussion]. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, 321(1207), 513–539.
- Romanowicz, R., & Young, P. (2003). Data assimilation and uncertainty analysis of environmental assessment problems—An application of Stochastic Transfer Function and Generalised Likelihood Uncertainty Estimation techniques. *Reliability Engineering and Safety System*, 79, 161–174.
- Rotmans, J., & van Asselt, M. B. A. (1996). Integrated assessment: A growing child on its way to maturity: an editorial essay. *Climatic Change*, 34, 327–336.
- Rotmans, J., & van Asselt, M. B. A. (2001a). Uncertainty in integrated assessment modeling: A lanarythic path. *Integrated Assessment*, 2, 43–55.
- Rotmans, J., & van Asselt, M. B. A. (2001b). Uncertainty management in integrated assessment modeling: Towards a pluralistic approach. *Environmental Monitoring and Assessment*, 69, 101–130.
- Sabel, C. E., Wilson, J. G., Kingham, S., Tisch, C., & Epton, M. (2007). Spatial implications of covariate adjustment on patterns of risk: Respiratory hospital admissions in Christchurch, New Zealand. *Social Science & Medicine*, 65, 43–59.
- Slater, D., & Jones, H. (1999). Environmental risk assessment and the environment agency. *Journal of Hazardous Materials*, 65, 77–91.
- Suter, G. W. I. I., Barnthouse, L. W., & O'Neill, R. V. (1987). Treatment of risk in environmental impact assessment. *Environmental Management*, 11, 295–303.
- Suter, G. W. I. I., Vermeire, T., Munns, W. R., & Sekizawa, J. (2005). An integrated framework for health and ecological risk assessment. *Toxicology and Applied Pharmacology*, 207, S611–S616.
- van Imhoff, E., & Post, W. (1998). Microsimulation methods for population projection. *Population: An English Selection. Special Edition: New Methodological Approaches in the Social Sciences*, 10, 97–138.
- van Maercke, D., & Defrance, J. (2007). Development of an analytical model for outdoor sound propagation within the Harmonoise Project. *Acta Acustica united with Acustica*, 93, 201–212.
- Walker, W. E., Harremoës, P., Rotmans, J., van der Sluijs, J. P., van Asselt, M. B. A., Janssen, P., et al. (2003). Defining uncertainty. A conceptual basis for uncertainty management in model-based decision support. *Integrated Assessment*, 4, 5–17.